## Accepted Manuscript

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PII: S1734-1140(17)30121-4

DOI: https://doi.org/10.1016/j.pharep.2017.09.008

Reference: PHAREP 797

To appear in:

Received date: 10-2-2017 Revised date: 8-9-2017 Accepted date: 29-9-2017

Please cite this article as: Mohamed A.Fouda, Hanan M.El-Gowelli, Sahar M.El-Gowilly, Mahmoud M.El-Mas, Hemin blunts the depressant effect of chronic nicotine on reflex tachycardia via activation of central NOS/PI3K pathway in female rats (2010), https://doi.org/10.1016/j.pharep.2017.09.008

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## ACCEPTED MANUSCRIPT

Hemin blunts the depressant effect of chronic nicotine on reflex tachycardia via activation of central NOS/PI3K pathway in female rats

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Running head: Nicotine interaction with reflex tachycardia.

**Supported by** the Science and Technology Development Fund (STDF), Egypt, Grant No. 502. The STDF had no role in the study design, in the collection, analysis and interpretation of data, in the writing of the report, or in the decision to submit the article for publication.

#### **Abstract**

**Background.** Chronic nicotine administration impairs reflex chronotropic responses that follow arterial baroreceptor unloading in female rats with repleted, but not depleted (ovariectomized, OVX), estrogen (E<sub>2</sub>). This study investigated whether products of nitric oxide synthase (NOS) and/or heme oxygenase (HO) and related soluble guanylate cyclase (sGC)/phosphatidylinositol 3-kinase (PI3K)/mitogen-activated protein kinases (MAPKs) signaling mediate the E<sub>2</sub>-sensitive depressant effect of nicotine on reflex tachycardia.

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